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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,626	08/04/2006	Philip Savage	30699/42250	7227

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
03/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,626	SAVAGE, PHILIP	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12-29-08&12-31-08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,22-25 and 28-37* is/are pending in the application.

4a) Of the above claim(s) *14-20,22-25 and 28-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 12-29-08 have been fully considered but they are not persuasive.

The amendments filed 12-29-08 and 12-31-08 have been entered. The amendment filed 12-31-08 corrects the status identifier of claim 1.

Claims 21, 26 and 27 have been canceled. Claims 1-20, 22-25 and 28-37 are pending.

Election/Restrictions

This application contains claims 14-20, 22-25 and 28-37 drawn to an invention nonelected without traverse in the reply filed on 4-30-08. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-13 are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Enablement

Claims 1-13 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is drawn to a method of damaging target cells in a mammal, the method comprising administering to the mammal: 1) a nucleic acid encoding portion of alcohol dehydrogenase (ADH) that converts ethanol to acetaldehyde; and 2) ethanol.

While the claims do not require therapy, the sole disclosed purpose for administering a nucleic acid encoding alcohol dehydrogenase and ethanol to a subject is treatment (pg 1, lines 6-13). The enablement rejection does not conflict with the art rejections because the art rejections are based on the claims, which do not require treatment. The enablement rejection is based on how to use the method claimed to treat disease in a subject. If other enabled uses for the method claimed besides treatment are disclosed, please point to them by page and line number.

At the time of filing Greco (J. Cellular Physiology, 2001, Vol. 187, pg 22-36) taught gene directed enzyme prodrug therapy (GDEPT) was known in the art by administering a vector encoding an enzyme of choice into tumor cells along with the enzyme's substrate that is converted into a toxic substance, which causes cell death (pg 23, Fig. 1). Using adenovirus for this type of treatment was known in the art at the time of filing (pg 28, 2nd full paragraph, last sentence; pg 28, col. 2, line 16, for example), and the promoter may be tumor-selective (pg 28, col. 1, 2nd full paragraph, line 5). Greco taught problems with gene therapy included delivery of a gene to the tumor, regulation of gene expression and therapeutic efficiency (pg 22, col. 1). All of the GDEPT described by Greco require direct injection into the tumor (see entire article); however, the claims at hand encompass any route of injection. Greco describes the desired features of the enzyme/prodrug combination on pg 23 and states several

combinations have been proposed for GDEPT, but most of them do not fulfill all the requirements including those in clinical trials (col. 2). Thus, it was unpredictable how to obtain a therapeutic effect using GDEPT at the time of filing.

The specification teaches administering transfected tumor cells then administered ethanol to mice (pg 61). The transfected tumor cells did not grow as fast as non-transfected tumor cells. Different cytotoxic effects were obtained depending upon the number of cells used (Fig. 1 vs. Fig. 2).

The specification teaches accurate assessment of cytotoxic effects of exposure to acetaldehyde is extremely difficult to quantify in vitro because acetaldehyde is volatile and because cells are able to metabolize acetaldehyde resulting in more rapid reductions in acetaldehyde dependant on the type and number of cells present (pg 63, lines 16-21).

The specification suggests using the method for treatment in vivo (pg 65-68) but does not teach how much ADH expression, ethanol or acetaldehyde are required to treat a pre-existing tumor or how to administer the nucleic acid in the absence of cells to obtain the same toxicity. Given the unpredictability of gene therapy in the art at the time of filing, taken with the teachings in the specification, it would have required those of skill undue experimentation to determine the parameters required to damage target cells in vivo using 1) a nucleic acid sequence encoding ADH and 2) ethanol as claimed.

Applicants argue the present invention meets all the requirements of Greco. Applicants' argument is not persuasive. Greco taught problems with gene therapy included delivery of a gene to the tumor, regulation of gene expression and therapeutic

efficiency (pg 22, col. 1). All of the GDEPT described by Greco require direct injection into the tumor (see entire article); however, the claims at hand encompass any route of injection. Greco describes the desired features of the enzyme/prodrug combination on pg 23 and states several combinations have been proposed for GDEPT, but most of them do not fulfill all the requirements including those in clinical trials (col. 2). Applicants have not provided any indication or evidence that they have overcome these obstacles. In particular, applicants have not taught how to target the nucleic acid encoding an enzymatically active portion of human alcohol dehydrogenase to tumor using any route of administration as broadly claimed. Without such guidance, applicants fail to enable those of skill to use the nucleic acid sequence claimed and ethanol to damage cancer cells or any other target cells.

Applicants' correction of the citation on pg 63, lines 16-21, is noted but does not address the basis of the rejection.

Applicants' sentence regarding dosage of ethanol is noted but does not address the basis of the rejection which is founded in the unpredictability of gene therapy.

Claim Rejections - 35 USC § 102

The rejection of claims 1 and 8 under 35 U.S.C. 102(b) as being anticipated by Mapoles (Alcoholism: Clinical and Exp. Res., May/June 1994, Vol. 18, No. 3, pg 632-639) has been withdrawn because the claims are limited to administering a nucleic acid and ethanol to a mammal while Mapoles is limited to administering a nucleic acid and ethanol to cells.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 4-9 and 8 under 35 U.S.C. 103(a) as being unpatentable over Philipott (Cancer Res. June 1979, Vol. 39, pg 2084-2089) in view of Greco (J. Cellular Physiology, 2001, Vol. 187, pg 22-36) and Yokoyama (Biochem. Biophys. Res. Communications, Aug. 30, 1994, Vol. 203, No. 1, pg 219-224) has been withdrawn because Philipott and Greco are limited to tumor cells in vitro while the claims require administering a nucleic acid and ethanol to a mammal.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Patent Examiner